

CLAIMS

We claim:

- Suba1*
- 5 1. A receptor molecule which binds to tumor necrosis factor comprising all or a functional portion of two or more extracellular domains of tumor necrosis factor receptors linked via one or more polypeptide linkers.
- 10 2. The receptor molecule of Claim 1 wherein the receptors are selected from the group consisting of: the extracellular domain of a p75 tumor necrosis factor receptor and the extracellular domain of a p55 tumor necrosis factor receptor or functional portions thereof.
- 15 3. The receptor molecule of Claim 1 further comprising a signal peptide of a secreted protein.
- 20 4. The receptor molecule of Claim 3 wherein the signal peptide is selected from group consisting of: the extracellular domain of the tumor necrosis factor receptor and a cytokine.
5. The receptor molecule of Claim 2 wherein the two or more tumor necrosis factor receptors are human.
- Suba2*
- 25 6. The receptor molecule of Claim 5 wherein the two or more extracellular domains of the tumor necrosis factor receptors are the same.
7. The receptor molecule of Claim 1 wherein the polypeptide linker is a polyglycine-serine linker.

Sub 8. Isolated DNA encoding a receptor molecule which binds to tumor necrosis factor, comprising two or more sequences encoding all or a functional portion of the extracellular domain of tumor necrosis factor receptors linked via one or more sequences encoding a polypeptide linker.

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9. The DNA of Claim 8 wherein the sequences encoding all or a functional portion of the extracellular domains of the tumor necrosis factor receptors are selected from the group consisting of: the sequence encoding the extracellular domain of the p75 tumor necrosis factor receptor and the sequence encoding the extracellular domain of the p55 tumor necrosis factor receptor or functional portions thereof.

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10. The DNA of Claim 8 further comprising a sequence encoding a signal peptide of a secreted protein.

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11. The DNA of Claim 10 wherein the sequence encoding the signal peptide is selected from the group consisting of: the sequence that encodes the signal peptide of the extracellular domain of tumor necrosis factor receptor and the sequence that encodes the signal peptide of a cytokine.

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12. The DNA of Claim 9 wherein the sequences encoding two or more tumor necrosis factor receptors are human tumor necrosis factor receptor.

13. The DNA of Claim 8 wherein the sequence encoding a polypeptide linker encodes a polyglycine-serine linker.

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Sub C2 14. The DNA of Claim 8 comprising SEQ ID NO: 1.

- Sub 4
15. A method of making a construct which expresses all or a functional portion of the extracellular domain of two or more tumor necrosis factor receptors linked via one or more polypeptide linkers comprising the steps of:
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- a) obtaining a first vector which expresses all or a functional portion of an extracellular domain of a first tumor necrosis factor receptor and a signal peptide of a secreted protein;
- b) obtaining a second vector which expresses all or a functional portion of an extracellular domain of a second tumor necrosis factor receptor; and
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- c) ligating the first vector of (a) to the second vector of (b) via a polypeptide linker
- so that the first vector of (a) is linked to the second vector of (b) via the polypeptide linker resulting in a construct which expresses all or a functional portion of the extracellular domain of the first tumor necrosis factor receptor and all or a portion of the extracellular domain of the second tumor necrosis factor receptor linked via the polypeptide linker.
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16. The method of Claim 15 further comprising the step of obtaining one or more vectors which expresses a second polypeptide linker and all or a functional portion of an extracellular domain of a third tumor necrosis factor receptor,
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- wherein the extracellular domain of the third tumor necrosis factor receptor is linked to the extracellular domain of the second tumor necrosis factor receptor via the second polypeptide linker.
17. Cells which express a receptor molecule which binds to tumor necrosis factor comprising all or a functional portion of the extracellular domain of two or more tumor necrosis factor receptors linked via one or more polypeptide linkers.
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18. A receptor molecule which binds to a cytokine comprising all or a functional portion of the extracellular domain of two or more receptors of the cytokine linked via one or more polypeptide linkers.

Sub A5 19. A method of inhibiting the biological activity of tumor necrosis factor comprising administering to a host an effective amount of a receptor molecule which binds to tumor necrosis factor, the receptor comprising all or a functional portion of the extracellular domain of two or more tumor necrosis factor receptors linked via one or more polypeptide linkers.

10 20. A method of treating or preventing a tumor necrosis factor related disease in a host in need thereof comprising administering to the host an effective amount of a receptor molecule which binds to tumor necrosis factor, the receptor comprising all or a functional portion of the extracellular domain of two or more tumor necrosis factor receptors linked via one or more polypeptide linkers.

15 21. A method of Claim 20, wherein the tumor necrosis factor related disease is selected from the group consisting of: an autoimmune disease, an inflammatory bowel disease, a bacterial infection, a viral infection, a parasitic infection, a malignancy, and a neurodegenerative disease.

20 22. A method of Claim 21 wherein the TNF related disease is selected from the group consisting of: rheumatoid arthritis, septic shock, cerebral malaria, inflammatory bowel disease, multiple sclerosis, allograft rejection, host versus graft disease, neoplastic pathology and endotoxemic response.

25 23. A method of Claim 20 wherein the tumor necrosis factor related disease is rheumatoid arthritis.

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